Claims 1, 2, 5, 6, 9, 10, 13 and 14 stand rejected under the judicially created doctrine of obviousness-type double patenting in view of Claims 1-23 of Levine et al (5,834,217). (see page 13 of the O.A.).

Claims 3, 4, 7 and 8 stand rejected under the judicially created doctrine of obviousness-type double patenting in view of Claims 1-23 of Levine et al (5,834,217) in view of Nagy. (see page 13 of the O.A.).

Claims 11 and 12 stand rejected under the judicially created doctrine of obviousness-type double patenting in view of Claims 1-23 of Levine et al (5,834,217) in view of Wardlaw (4,156,570). (see page 14 of the O.A.).

THE 35 U.S.C. 112 REJECTIONS:

This rejection does not conform to USPTO standards since it is set forth in an "and/or" format (see page 2, part 2, line 3 of the O.A.). Pages 2-9 of the office action contain twenty separate rejection paragraphs which apparently are grounded on either paragraph 1 or paragraph 2 of §112 of the statute. None of the aforesaid rejection paragraphs specify which paragraph of §112 of the statute provides grounds for such rejections. Furthermore, five of the rejection paragraphs do not specifically refer to any of the claims in the claim set 1-14 which are being rejected by the arguments put forth in said five rejection paragraphs. It is respectfully submitted that an Examiner cannot put the onus on an applicant, in a response to an office action, to try to guess what the statutory basis for any particular rejection is. Paragraph 1 and paragraph 2 of §112 of the statute are separate and distinct sections of the law and cannot be intermingled by an Examiner.

A few further observations regarding this set of rejections put forth by the Examiner.

The Examiner has made repeated references to "one of skill" in proffering the §112 rejections, but has never come to grips with the question of what art is the "one of skill" that she continuously refers to, skilled in. The "art" is clearly cytology or cell pathology,

or the art of distinguishing one cell type from another. See, for example, page 1 of the specification. In essence, in many of the rejections, the Examiner is making the argument that a skilled cytologist would not know what an abnormal cell looks like, and would not recognize abnormal cell morphology. If this were indeed the case, why would a physician order a biopsy of tumorous tissue?

The Examiner has used the term "confusing" repeatedly in the grounds for rejection. Is the Examiner saying that she is confused by the claims, or that one skilled in the art would be confused by the claims? Why are the claims confusing? Why would one skilled in the art not know what the claims encompass, and thus what they preclude one from doing?

We would advise the Examiner to look to the specification to see whether it offers guidance as to the claim language. Claims cannot be read in a vacuum, but must be read in light of the application's disclosure and the teachings of prior art; the second paragraph of 35 USC 112 requires merely that claims set forth and circumscribe particular area with reasonable degree of precision and particularity, and that applicants claim that which they consider to be their invention. See: Ex parte Calhoun and Bennett, 195 USPQ 455 (PTO Bd. App. 1976); and In re Johnson and Farnham, 194 USPQ 187 (CCPA 1977).

With all due respect, the §112 rejections include some grounds which seem to the undersigned to be facetious. One of these rejections is put forth on pages 5 and 6 of the office action wherein the Examiner alleges that the recitation of "constituent components of blood" is vague and indefinite because it is not clear what is encompassed by this term ("phrase"?). Is the Examiner suggesting that a skilled cytologist would not know what constituent components of blood are? What are the Examiner's grounds for this suggestion?

The most disingenuous ground for rejection of a claim is found on page 7 of the office action wherein the Examiner alleges that Claim 10 is vague and indefinite because it would not be not clear to one skilled in the cytology art what a "microscopical

instrument" is. The Examiner asks whether a "microscopical instrument" as used in conjunction with this invention: "Is +++ an extremely tiny instrument of some sort?". The term "microscopical" is the preferred adjective for use in describing an instrument used in the field of microscopy. We would advise the Examiner to check out a dictionary on this point. What does the Examiner see in the specification that suggests to her that "an extremely tiny instrument" should be used in performing the method of this invention?

The grounds for rejection of Claims 4-6, 9 and 13 contained on page 6 of the O.A. suggest that the Examiner is seeing the word "only" somewhere in these claims as related to the nucleated cells. The claims do not state that only nucleated cells accumulate in the "well-defined zone" in the tube. Likewise, Claim 6 does not require that normal blood cells be excluded from the "well-defined zone" in the tube. The Examiner's analysis of these claims which is contained on page 6 of the O.A. is thus clearly erroneous.

The term "differentiated" is a common term in the English language, and simply means to "mark or show a difference". Again, please consult a dictionary.

To sum up the undersigned's comments regarding the §112 rejections, please note the following:

1) The scrambled format in which these rejections, Para. 1 and Para. 2, were put forth does not meet USPTO requirements for clarity;

2) The Examiner's failure to consider the level of skill of a cytologist or cell pathologist (one skilled in this art) in identifying abnormal cells, such as cancer cells, which may be found in a circulating blood sample, and in identifying conventional blood constituents which will certainly be found in the blood sample constitutes clear error;

3) Again, with all due respect, certain of the noted §112 grounds for rejection are silly; and

4) The level of one skilled in the art in question must be taken into account in rejecting claims under this part of the statute. The clarity of the disclosure and the metes and bounds of the claimed subject matter must be measured against the knowledge of one skilled in the art in question, and not against the knowledge of the art in question which is possessed by a patent examiner.

THE 35 U.S.C. 102 REJECTIONS:

These rejections are based on two patents, one of which is the '217 patent to Levine et al, and the other of which is the '362 patent to Levine et al. The grammar used on page 10 of the rejection is not crystal clear, however it appears that the Examiner is using the aforesaid two references in concert in the proffered §102 rejections. The '217 patent is a divisional of the '362 patent, thus both patents have the same effective filing date, i.,e., May 23, 1994, and both have identical disclosures. In view of the above, the Examiner should not use both of the patents in the §102 rejections. One will do. In responding to the §102 rejections, the undersigned will refer to the '217 patent.

It is noted that Claims 1, 2, 5, 6, 9, 10, 13 and 14 have been rejected as being anticipated by the '217 patent. The factual determination of anticipation requires the disclosure in a single reference of every element of the claimed invention. See: Ex parte Levy, 17 USPQ2d 1461 (PTO Bd. of Pat. App. and Int. 1990). Furthermore, it is encumbent upon the examiner to identify wherein each and every facet of the claimed invention is disclosed in the applied reference. See Lindermann Maschinenfabrik GmbH v. American Hoist and Derrick, 221 USPQ 481 (Fed. Cir. 1984).

In the instant case, Claims 1, 2, 9, 10, 13 and 14 all require the examination of cell morphology *in situ* in the tube. This step is not suggested by the '217 patent and is not possible with the equipment described in the cited patent. The cited patent describes an assay of a blood sample **for bands** of target analytes which are captured by capture bodies such as liposomes (see Col. 2 of the patent). Thus the cited patent cannot be said to anticipate any of Claims 1, 2, 9, 10, 13 and 14. This rejection is

therefore clearly erroneous.

Claims 5 and 6 both recite the differentiation of cancer cells and hematologic progenitor cells from each other and from other nucleated cells in the blood sample. Note that Claims 5 and 6 are included in the Claim 1-10 group which stand rejected in part 7 of the office action.

The '217 patent does not refer at all to the detection of cancer cells, a fact that the Examiner admits in part 7 of the office action relating to the §103 rejection of Claims 5 and 6. Thus the §102 rejection is clearly erroneous, and the grounds for the §102 rejection of Claims 5 and 6 are clearly refuted even by the Examiner's own comments contained in the subsequent §103 rejection put forth in the office action.

THE 35 U.S.C. 103 REJECTIONS:

PARA. 7. 0.A.: Claims 1-10, 13 and 14 stand rejected as being obvious over Levine et al '217 in view of Nagy. The Examiner states that Nagy teaches that epithelial cancer cells are found in the white cell layer of a centrifuged sample of blood, and that it would be obvious to extend the method of Levine et al to the detection of any nucleated cell with a reasonable expectation of success since cancer cells are known to be present in the white cell layer of the centrifuged sample of blood.

The Nagy reference uses a centrifuged concentrate of white cells which are smeared on a slide and examined under a microscope. In order to be able to study the morphology of a cancerous epithelial cell, the power of the microscope would have to be at least 100X. Cancer cells are identified in Nagy in the smear by their abnormal intracellular morphology.

The Levine et al '217 reference describes a blood analyzing system and method which uses an instrument that can detect and measure differentially colored blood constituent layers or bands of cells in a centrifuged blood sample. The '217 patent in describing the instrument that it employs refers to U.S. Patent No. 4,558,947 (See Col. 11, line 38 of '217), and the '947 patent in turn refers to U.S. Patent No. 4,156,570,

(which the Examiner has cited in this case) in describing the instrument used in the analysis. The '570 patent teaches the use of a lens system for use in measuring the blood constituent bands, which lens system has a range of magnification of from 4 to 20X (See Col. 4, line 59). Thus, the '217 blood analyzing system uses an instrument which has a range of magnification of from 4 to 20X. An instrument with this range of magnification would not be able to detect any nucleated cells, including epithelial and cancer cells in the centrifuged blood sample. Such an instrument would also not be able to analyze cell morphology. One must bear in mind that the "QBC" instrument described in the Wardlaw patents **sees cell bands, it does not see individual cells**. If one were to increase the power of the '217 optical system to the minimum of 100X which is needed to identify abnormal cells by the procedure described in Nagy, then the resultant '217 modified instrument would not be able to detect the cell bands in the blood sample, thus it would be rendered useless for the procedure for which it was created in the first place. Stated another way, the instrument wouldn't be able to see the forest for the trees if it were equipped with at least a 100X magnification lens set.

One final point. None of the references cited by the Examiner recognizes the fact that centrifuged cancer or progenitor cells will gravitate to a location which is in close proximity to the platelet layer in a centrifuged sample of whole blood. White cells and platelets are not the same animal.

PARA. 8, O.A.: Claims 11 and 12 stand rejected as being obvious over '217 in view of Wardlaw '570. The Examiner states that the '570 patent teaches the use of a microscopical instrument having a focal operating range that enables the measurement of a transverse section of 10-100 microns in a specimen being examined. This allegation is totally unfounded. As noted above, the '570 patent describes an instrument which needs only to focus on the surface of the cell bands in a tube. The focal operating range of the '570 instrument is not specified in the patent, and is irrelevant to operation of the '570 patent instrument. The Examiner cites Col. 1 of the '570 patent in support of the grounds for rejection, citing something about "error" in that column of the patent. The only "error" referred to in Col. 1 of the patent is the

irregular interface between cell bands, and that "error" is corrected by spinning the tube in the instrument.

The §103 rejections put forth in the office action are not well taken and should be withdrawn.

THE DOUBLE PATENTING REJECTIONS:

Claims 1-10, 13 and 14 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-23 of the '217 patent, and, regarding certain of the rejected claims further in view of Nagy. Claims 11 and 12 also stand rejected under the obviousness-type double patenting doctrine over Claims 1-23 of the '217 patent and the '570 patent.

All of the double patenting rejections are based on Claims 1-23 of the '217 patent. It is respectfully submitted that a double patenting rejection does not lie in this case. The application being examined is the product of four inventors, i.,e., Rimm, Levine, Wardlaw and Fiedler. This application is owned by the inventors Levine and Wardlaw due to an assignment from the other two inventors. Becton Dickinson and Company has no ownership rights to this application.

The '217 patent is the product of ten different inventors, two of whom are Levine and Wardlaw, and the rest of whom are employees of Becton Dickinson and Company. The '217 patent is co-owned by Becton Dickinson, and by Levine and Wardlaw, jointly. Thus the instant application and the '217 patent are not commonly owned. A double patenting rejection requires common ownership of the rejected application and of any patent forming a basis of the double patenting rejection.

The double patenting rejections put forth by the Examiner in this case are thus not supported by law, and must be withdrawn.

Regarding the use of the "QBC" trademark designation in the specification is believed to adequately protect the trademark. Should the Examiner believe otherwise, please

point out specific instances wherein the guidelines have not been met.

In view of the above-noted arguments, it is respectfully submitted that the Examiner must reconsider the grounds for rejecting the claims in this application and issue a new office action.

It is noted that the drawings submitted in this application have not been objected to.

Respectfully submitted,

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